

REMARKS

This paper is respectfully filed pursuant in response to the Final Rejection rendered February 8, 2007. It is timely in view of the Petition for Extension of Time and Request for Continued Examination filed concurrently herewith. Applicants have also filed concurrently herewith a Supplemental Information Disclosure Statement as well as best available copies of the documents set forth in the Information Disclosure Statement submitted on December 4, 2006.

Claims 1-22 and 68-75 are pending. Claim 1 has been amended to specify the description of the methods of applicants' invention. Claims 72-75 have been added. Basis for the amendment to claim 1 and new claims 72-75 may be found in the Specification at p. 21, l. 20 to p. 23, l. 20 and in Figures 4 and 5.

The Final Rejection of February 8, 2007 indicates that the Information Disclosure Statement filed December 4, 2006 failed to comply with 37 CFR 1.98(a)(2) in that the copies of non-U.S. documents submitted were not legible. Applicants respectfully submit that such documents were legible and believe that translations were submitted, however, they are respectfully re-submitting the Supplemental Information Disclosure Statement and attachments herewith.

The Final Rejection of February 8, 2007 rejected claims 1-22 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The basis for this rejection was stated as follows:

...the claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is new matter rejection. {Final Rejection, p. 3]

The Final Rejection further stated that:

...claim 1 directs that after daily application of the serine protease containing composition for at least 4 weeks, hair growth, hair follicle and hair shaft size are reduced. However, the specification does not provide support for reduction of hair growth, hair follicle and hair shaft. The example 4, daily treats hair with soy-milk. Hair pigmentation determination was done at days 7-8 and day 11-12. Page 17, lines 11-17 describe applying the composition to the skin daily for four weeks and for eight weeks. This paragraph does not state determination of hair-growth or hair pigmentation after the times disclosed. [Final Rejection, p. 3]

Applicants respectfully request reconsideration of this rejection in view of the ensuing remarks and the foregoing amendments to the claims.

Applicants respectfully submit that there is ample basis for the subject matter set forth in claim 1 as amended previously—they are not required to exemplify every embodiment of the claimed invention. However, in order to expedite prosecution and clarify the methods of the invention, applicants have amended claim 1 to indicate that, as fully exemplified in, but not limited to Examples 4 and 9, *inter alia*, application of the compositions of the invention to hair for at least seven days from the beginning of the hair cycle results in reduction of hair growth, hair follicle size and hair shaft size. These effects are amply illustrated in Examples 4 and 9 as well as in Figures 2, 3, 4, 5 and 15, which represent gross and microscopic depictions of the reduced hair growth, hair follicle size and hair shaft size resulting from following the methods of applicants' invention.

Applicants respectfully submit that following the methods of their invention would have been understood by those of ordinary skill in the art to continue producing the illustrated results so long as the methods are followed, i.e., on a continuing basis. Applicants respectfully suggest that evidence of such ongoing results are unnecessary to support their claim and that such results are fairly extrapolated from the data provided in the Specification—otherwise, patent applicants would be required to continue performing claimed methods for an indeterminate period of time before filing their applications. Applicants respectfully submit that there is adequate basis in the Specification for continuing to observe results subsequent to the experimental period. Applicants therefore respectfully request reconsideration of the rejection under 35 U.S.C. 112, first paragraph in view of the foregoing discussion.

The Final Rejection of February 8, 2007 again rejected claims 68 and 69 under 35 U.S.C. 103(a) as being unpatentable over Costanzo (US 6,323,219) in view of Matsuura et al. (US 6,139,899). The basis for this rejection was that Costanzo:

...discloses method and composition for "bringing about skin pigmentation and/or for causing skin depigmentation;"...The composition of Costanzo contains serine protease inhibitors that may be obtained from extracts of Solanaceae, Gramineae, Cucurbitaceae and Leguminosae...soybean milk also contains serine protease..." [Final Rejection, p. 3-4]

The Final Rejection further states that:

Costanzo specifically discloses topically applying to mammalian skin pharmaceutical or cosmetic composition in an amount effective to effect changes in pigmentation...and soybean milk or other formulations derived directly from legumes is applied to the mammalian skin... [Final Rejection, p. 4]

In addition, the Final Rejection argues that:

The instant method involves topical application to the skin a topically active composition that comprises one or more compounds derived from one or more of the botanical families. Since the instant method topically applies a composition and Costanzo topically applies to the skin a composition that reads of the instant composition, it would be inherent that the composition of the prior art affects the skin the same way as the instant composition affects the skin...Thus, although Costanzo does not specifically disclose that the composition has an effect on hair growth, since the instant claim 1 and Costanzo apply the same composition to the skin, the effect on the skin from both compositions would be the same. [Final Rejection, p. 4]

Applicants respectfully request reconsideration of this rejection in view of the ensuing discussion.

Applicants again respectfully submit that Costanzo neither suggests nor describes methods for using the composition of applicants' invention to affect hair growth. Applicants respectfully call attention to the fact that skin and hair pigmentation are not identical. For example, hair color might turn gray upon aging, but skin color does not show a similar effect.

Moreover, it is well-known that hair growth is not related to hair color; both naturally-pigmented hair and gray (non-pigmented) hair can grow to different lengths and thicknesses. "Hair appearance" includes not only color, but also hair density, thickness and length, and the appearance of hair in undesired locations (e.g. female facial or leg hair, male beard area).

As set forth in the claims, Applicants make clear that according to applicants' methods, the composition is to be applied to *mammalian hair in need of a change in appearance*, emphasizing the reduction in visibility of unwanted hair growth by reducing hair follicle dimensions and reducing the growth rate of the hair shaft.

Costanzo, however, suggests the opposite, i.e., *darkening gray hair*. While Costanzo is a composition of melanin combined with a *phagocytosis-enhancing* agent, intended to induce coloration of gray hair, the compositions and methods of applicants'

invention use trypsin **inhibitory** activity to reduce the visibility of undesired hair, to thin hair, to slow hair growth, and to enable management of “difficult hair” (e.g. Afro American hair, pseudofolliculitis barbae hair) by slowing hair growth parameters.

Applicants respectfully submit that Costanzo neither explicitly nor inherently describes or suggests the methods and compositions of applicants’ invention. As set forth in the ensuing discussion, Costanzo’s only reference to use of **any** composition on hair relates to a composition **different** from that set forth in applicants’ claimed invention. Moreover, Costanzo’s topical use on the skin of compositions containing soymilk, for example, would not have inevitably led to use of the methods of applicants’ claimed invention. There are many areas of the skin that would not contain hair in need of a change in appearance, such as the female face.

The only statement set forth in Costanzo that relates to hair treatment is as follows:

Skin disorders include unwanted pigmentation, unwanted depigmentation, psoriasis, rashes, and certain physical skin imperfections (e.g., wrinkles). In one specific example, vitiligo patients are treated with melanin (via liposomes or plain) together with a phagocytosis-increasing agent (e.g., SLIGRL) to darken the light spots. Alternatively, they are treated with Compound I to lighten the darker sites (see U.S. Ser. No. 09/110,409, filed Jul. 6, 1998). ***In an example related to skin disorders, gray hair is treated with melanin (plain or liposome-delivered) and phagocytosis-increasing agent (e.g., SLIGRL), ideally in a shampoo or cream.*** Central nervous system disorders include, without limitation, Alzheimer’s disease and other senile plaque disorders (treated via up-regulating the phagocytosis of amyloid fibrils), depression, phobic disorders, and other disorders resulting from secondary effects of benzodiazepine treatment. [Costanzo, col. 30, l. 14-32] (emphasis added)

Clearly, Costanzo distinguishes between treating darker skin sites with trypsin inhibitory products such as Compound I and darkening gray hair using SLIGRL, a **PAR-2 agonist and phagocytosis-increasing agent**.

Thus, the only suggestion in Costanzo for use of compositions on hair requires treatment of gray hair with melanin and a phagocytosis-**increasing** agent, SLIGRL. SLIGRL is not a member of the botanical families set forth in the compositions of applicants’ invention. It is a **phagocytosis enhancer** applied in conjunction with melanin, **not** a serine protease inhibitor. Thus, Costanzo does not suggest or describe the application of compositions of applicants’ invention on **hair**.

Even if one were to follow Costanzo in applying compositions topically to skin, the result would not *inevitably* be that of the methods of applicants' invention, as required in order to serve as a basis for an inherency rejection.

All pigment in the hair arises from the hair bulb from a line of melanocytes that produces the melanosomes for the keratinocytes of the hair shaft. Pigment is added to the hair only during the growing or anagen stage. There is no pigment production during the resting or telogen stage. The perceived color of hair is the result of structural proteins, the luminance and color dilution. [*Physiology of the Skin II*, Peter Pugliese, Chapter 5, p. 54 (2001)] . Thus, mere application of the compositions set forth in Costanzo to skin at certain times during the life cycle of a hair would not necessarily inevitably effect changes in a hair that may be located in proximity to the skin being treated if they are applied indiscriminately during the life cycle.

Moreover, Costanzo's only reference to hair itself relates to darkening gray hair, but not to reducing hair color or visibility. It clearly does not mention any effect on hair growth parameters. Indeed, the only effect on gray hair set forth in Costanzo is providing *exogenous* melanin to "stain" gray hair. In contrast, the methods of applicants' invention perform the opposite, i.e., reducing hair visibility by reducing growth and *endogenous* melanin production, or reducing hair growth to manage making it grow slower, and appear thinner.

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Applicants respectfully submit that Costanzo does not teach the methods of claims 68 and 69. These claims are directed to methods for effecting changes in mammalian hair appearance and hair pigmentation, and reducing hair growth, and hair follicle and hair shaft size by a topical application of a topically active composition containing one or more compounds derived from one or more botanical families

leguminosae, solanaceae, gramineae and cucurbitaceae. Costanzo does not meet these limitations and therefore does not anticipate the invention. Nor would it be inherent that the invention of Costanzo would affect the hair as required by the rejected claims. Applicants therefore respectfully request reconsideration of the rejection under 35 U.S.C. 103(a) in view of Costanzo.

Claims 70 and 71 were rejected under 35 U.S.C. 103(a) as being unpatentable over Miljkovic (US 5,985,842) on the ground that:

Miljkovic describes a method of reducing hair growth by topically applying composition that comprises boron compound as a solution or emulsion in soybean oil or bile acid salt as carrier; the composition penetrates the skin stratum corneum barrier to reach the hair follicle root...While it is known in the art that soybean oil contains trypsin inhibitory activity (see Kridl...as a teaching reference for soybean oil containing trypsin inhibitory activity). **Miljkovic does not disclose the soybean containing composition to reduce hair pigmentation.** However, since the composition is applied topically to the skin effect reduction in hair growth, the composition would inherently produce other effects such as reduction in hair pigmentation, reduction in hair follicle and hair shaft. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to apply the composition of Miljkovic to the skin to reduce hair growth and expect to obtain other benefits of the soybean oil containing composition on the skin and on the hair follicle root. [Final Rejection, p. 6] (emphasis added)

Applicants respectfully request reconsideration of this rejection in view of the ensuing discussion.

Applicants respectfully submit that the Miljkovic nowhere suggests or teaches that soybean oil or, indeed, **any** soybean derivative would affect the appearance of hair. Miljkovic relates to the use of boron compounds or complexes to regulate hair growth [Miljkovic, col. 1, l. 1-2]. The presence of soybean oil in the formulations is merely suggested by Miljkovic as one of several recommended carriers for the boron compounds [Miljkovic, col. 5, l. 16-39]. Nowhere is there a suggestion in Miljkovic that the carriers set forth therein are active ingredients in the formulations. Thus, the presence of soybean oil in the formulations of Miljkovic is merely coincidental and would not have directed one of ordinary skill in the art toward the methods and compositions of applicants' invention.

Even if Miljkovic might have suggested the use of soybean oil in hair regulating compositions, the patent would still not have directed one of ordinary skill in the art toward the active hair-regulating compositions of applicants' invention. Soybean oil is a refined derivative of the soybean and is not known to contain soy trypsin inhibitors. Thus, a composition containing soybean oil would not have been active in regulating the growth and appearance of hair.

The Final Rejection relies upon the Kridl patent as teaching that one of skill in the art would have known that soybean oil contains trypsin inhibitory activity. However, Kridl relates to improving soybean-based products for use in food [Kridl, col. 4, l. 15-24] via "a method for increasing stearate as a component of total triglycerides found in soybean seed". [Kridl, Abstract] While it mentions the presence of trypsin inhibitors in *soybean seeds* that contain the desired oils for the soybean oil compositions of the Kridl invention, it specifically teaches **removing** the trypsin inhibitor from the preparations made from the soybeans seeds that serve as the source for the soybean oil compositions (see below). Furthermore, the Kridl patent specifically relates to reducing the "need for industrial hydrogenation of polyunsaturated oil for food applications...by the preparation of soybean oil with increased concentrations of stearate." [Kridl, col. 4, l. 20-23] Thus, Kridl is concerned with **ingestible** soy-containing products. Such products cannot contain trypsin inhibitors or they would be indigestible and cause gastric distress to those who eat them.

The Kridl patent, moreover, teaches the *removal* of soy trypsin inhibitors from food products relating to the soy. Rather than demonstrating that soybean oil contains trypsin inhibitors, Kridl merely states that the *soybean seeds that are a source of the oil* contain trypsin inhibitors, as follows:

Alternatively, the *soybean seeds* containing the modified fatty acid compositions of the present invention may be used to prepare soymilk...The heating step may comprise heating the mixture to any temperature suitable for the formation of tofu, ***preferably to a temperature sufficient to inactivate the trypsin inhibitor*** in the liquid at least about 80% as compared to the trypsin inhibitor activity prior to heating, and most preferably to a temperature between about 90° and about 100° C...

Soybean seeds containing the novel soybean oil compositions of the present invention may find use in the preparation of tofu...The heating step may comprise ***heating the mixture to any temperature suitable for the formation of***

tofu, preferably to a temperature sufficient to inactivate the trypsin inhibitor in the liquid at least about 80% as compared to the trypsin inhibitor activity prior to heating, and most preferably to a temperature between about 90° and about 100° C. [Kridl, col. 10, l. 31-66] (emphasis added)

Thus, Kridl does **not** teach that one of ordinary skill in the art would have known that soybean oil contains trypsin inhibitory activity. In contrast, it teaches away from that proposition—it suggests that soybean oil and other soy derivatives should be treated to **remove** trypsin inhibitors. Thus, Kridl may not be utilized to demonstrate that the Miljkovic patent would have taught one of ordinary skill in the art toward the compositions and methods of applicants' invention based upon its boron compound and soybean oil-containing compositions set forth therein. Applicants therefore respectfully request reconsideration of the rejection of claims 70 and 71 under 35 U.S.C. 103(a) as being unpatentable over Miljkovic.

Therefore, in view of the foregoing discussion and amendments, Applicants respectfully request reconsideration of the rejections set forth in the Final Rejection of February 8, 2007. An early allowance is earnestly solicited.

Respectfully submitted,

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